Brain development: **Lightning is always seen, thunder always heard**

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An old suggestion that crossing the visual and auditory pathways to the brain would lead to light being experienced as sound, and *vice versa*, has been tested and found to be false.

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Over a century ago, the psychologist William James proposed a thought experiment, and suggested the answer: if the eyes were forced to connect to the auditory centres of the brain, and the ears with the visual centres, we would "hear the lightning and see the thunder" [1]. James' point was that the perceptual qualities of our sensations — what philosophers term qualia — have their origin in the brain's central neural mechanisms, rather than in the particular physical properties of sound and light, or in the sensory receptors of the eye and ear. While this seems reasonable, a critical question remains: are the types of sensory processing that ultimately give rise to qualia innately determined properties of different cortical areas, or are they the secondary outcome of a general purpose learning algorithm applied to sensory inputs which have a different information content? If the former is the case, James' conjecture would hold, if the latter, it need not, once learning had taken place.

An answer supporting the latter possibility comes from an elegant set of experiments done on ferrets by Mriganka Sur and his colleagues [2,3]. They have shown that if retinal inputs are forced to innervate the auditory cortex at birth, it develops in a way that is much more like visual cortex than auditory cortex. Furthermore, the visually driven auditory cortex can not only mediate visually guided behaviour, but behavioural tests show that the percepts induced by visual stimulation appear to be visual rather than auditory — that is, lights are seen rather than heard by such animals.

These experiments have their origin in work by Schneider [4] and Frost and Metin [5] showing that different thalamic nuclei — each of which sends sensory information to a specific area of cortex — can be innervated by the wrong set of sensory afferents, provided the afferents which would normally have innervated the nucleus are removed at a sufficiently early stage in development. In the experiments of Sur and colleagues [2,3], the afferents to the part of the thalamus that normally relays auditory inputs to the auditory cortex were removed at birth, with the result that the auditory thalamus was taken over by inputs from the eye (Figure 1). The ferrets were then raised normally until adulthood. Previous work on such rewired animals has shown that cells in what would have become auditory cortex have now acquired properties similar to those of normal visual cortex neurons. For example, they have receptive fields in localised regions of visual space and they show orientation and direction selectivity — that is, they respond best to contours of a particular orientation moving across the receptive field [6]. As in visual cortex, there is also an orderly topographic map of visual space [7].

New data have added to the list of similarities. In the normal visual cortex, the preferred orientations of neurons change in an orderly way across the surface of the cortex. The resulting orientation map is locally continuous

Figure 1

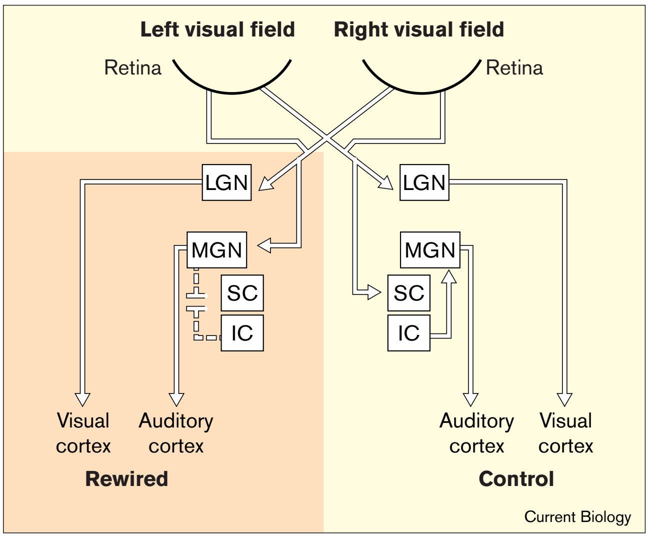
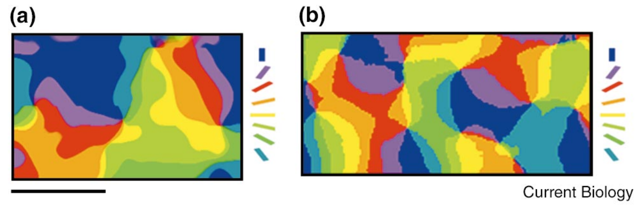


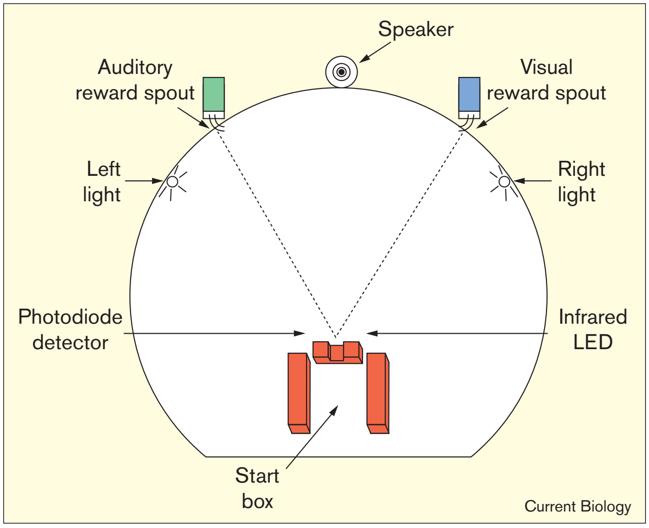
Diagram showing the pathways between eye and brain in a rewired ferret. The projection from the left visual field to the right side of the brain is normal: pathways from the left nasal retina and the right temporal retina go to the visual thalamus (LGN) on the right hand side, and then to the right visual cortex. Auditory pathways on this side go from the inferior colliculus (IC) to the auditory thalamus (MGN) and then to auditory cortex. On the left (rewired) side of the brain, the pathway from the inferior colliculus (IC) to the auditory thalamus (MGN) has been surgically interrupted and the superior colliculus has been removed. The MGN receives an aberrant projection from visual pathways subserving the right visual field. In the behavioural tests, the LGN on the left side was lesioned, so that the only source of visual input to the left side of the brain was via the MGN and auditory cortex. (Adapted with permission from [3].)

Figure 2



Colour-coded maps of orientation preference obtained by optical imaging in the ferret: **(a)** from rewired auditory cortex; **(b)** from normal visual cortex. Scale bar equals approximately 1 mm. (Adapted with permission from [2].)

Figure 3



Apparatus used for behavioural testing: the ferret initially has its head facing directly forward in the start box (detected by the photodiode). The ferret is trained to go to the reward spout on the left following an auditory stimulus and to the right following a visual stimulus. (Adapted with permission from [3].)

— neighbouring neurons tend to prefer similar orientations — and it is periodic — on average, regions containing cells whose orientation preferences lie within a certain range (iso-orientation domains) are spaced about a millimetre apart. Another distinctive feature of these orientation maps is the frequent occurrence of singular points, which resemble pinwheels in colour plots, around which a single complete set of orientation domains meets. Tracer injection studies have also revealed a network of patchy tangentially distributed axons that connect regions with similar orientation preference up to several millimetres apart [8].

It has now been shown [2,9] that all of these distinctive visual cortex features are present in the rewired auditory cortex (Figure 2). They have presumably arisen *de novo*, because nothing resembling them occurs in normal auditory cortex: normally it contains a map in which stimulus frequency is represented in parallel iso-frequency bands, and local intra-cortical connections extend for relatively short distances along the bands. The important conclusion is that, when subjected to patterns of input activity driven by visual stimuli, the auditory cortex develops circuitry which is similar to that normally found in the visual cortex. The map topography and details of the circuitry thus appear to be determined by the input activity patterns, rather than by the intrinsic properties of auditory cortex.

Even more interesting than this perhaps, is the answer to James' question: do rewired ferrets experience visual stimuli as sound or as light? This question might seem unanswerable (even in principle, and especially where ferrets are concerned) but it can be answered, by taking advantage of the fact that behavioural responses to stimuli tend to be generalised along dimensions that are perceptually similar. For example (Figure 3), it is possible to train a ferret to move to the right when a light is presented in the left visual field, and to the left when a sound stimulus is presented (the location of the sound is not critical). When a light is now presented in the right visual field, the ferret will move to the right, because of the perceptual similarity of lights presented in either the right or the left visual field. Von Melchner *et al.* [3] used this technique with ferrets in which the auditory cortex on only the left side of the brain had been rewired (as in Figure 1).

Von Melchner *et al.* [3] found that, after training these ferrets to move to the right when a visual stimulus was presented in the left visual field (which was processed only by the normal visual pathways on the right side of the brain), and to the left in response to a sound stimulus (processed by the remaining normal auditory pathways on the right side of the brain), the ferret responded to a light presented in the right visual field (now processed only by the rewired auditory cortex) by moving to the right. This behavioural response indicated that a visual stimulus processed by the rewired auditory cortex was perceived as more similar to a visual stimulus processed by visual cortex than to a sound stimulus processed by normal auditory cortex. (Sceptics wishing to search for flaws in the argument should consult the original publication for details of additional confirmatory tests.)

The conclusion then, is that different cortical areas are not restricted in terms of the types of computation they can carry out. Secondly, it would appear (and one can argue that it must necessarily be the case) that percepts are determined by the type of cortical processing that sensory inputs receive — in contemporary jargon, the computational structure of the analysis — rather than by the specific piece of neural tissue that does the analysis. One objection to this is that the rewired auditory cortex may have managed to redirect its outputs to higher level visual areas, which remain the ones which mediate the percepts. In fact tracer studies show that the rewired auditory cortex maintains the connections it would normally have had with other auditory cortical areas [10], although this does not rule out the possibility that higher-order connections might have changed.

Many readers will recognise these new findings as the latest salvo in an ongoing battle between two opposing views of cortical development. On one side is the nativist view that the specific structural details of the various types of functional map found in cortex are innately determined, and that experience driven neural activity has mainly a maintenance function. On the other, is the empiricist view that, at birth, the cortex is a *tabula rasa*, and that the various different forms of organisation are the outcome of a general purpose learning algorithm acting on different patterns of activity in the different sensory afferent pathways.

Intriguingly, both sides in the argument can call on considerable bodies of evidence to support their points of view. Nativists can point to the fact that many forms of cortical organisation develop without environmentally driven stimulation. For example, orientation columns are present at birth in the monkey and oriented patterns of activity driven by naturally occurring edges are not a prerequisite for their formation. Other structures, such as ocular dominance columns, may form in the absence of the eyes [11], and identical orientation maps for each of the eyes may form, even when the eyes never had simultaneous visual experience [12].

Empiricists can point to the large body of evidence showing that abnormal forms of visual experience can radically change the outcome of visual cortex development — see, for example, the latest evidence that selective exposure in early life to contours of one orientation causes the orientation preferences of many visual cortex neurons to shift to the experienced orientation [13]. Experiments done early in cortical development show that areal boundaries are not fixed and that transplanted cortical tissue takes on the characteristics of the region to which the tissue is transplanted rather than retaining those of the donor region [14].

Although the results from the rewired ferret [2,3] clearly support the empiricist view, they certainly do not rule out an innate predisposition of particular cortical areas to form structures which are best suited to the inputs they would normally receive. This would make evolutionary sense, because new-born animals would gain a head start in learning about the world. Nevertheless, the experiments suggest, perhaps more clearly than any done previously, that these early developmental programs are predisposing, rather than determinative. They imply a close relationship between cortical map structure and the properties of the natural world. They also neatly demonstrate that the lightness of lightning and the thunderousness of thunder are determined by the brain's computational analysis, rather than by where it is done, or by what type of neural tissue.

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